Auditory brain-stem responses in syphilis

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SUMMARY Analysis of auditory brain-stem electrical responses (BSER) provides an effective means of detecting lesions in the auditory pathways. In the present study the wave patterns were analysed in 11 patients with secondary or latent syphilis with no clinical symptoms referrable to the central nervous system and in two patients with congenital syphilis and general paralysis. Decreased amplitudes and prolonged latencies occurred frequently in patients with secondary and with advanced syphilis. This technique is a notable diagnostic advance in detecting syphilitic damage of the brain stem.

Introduction

Because of the effects on the cardiovascular and nervous systems syphilis is a serious infectious disease. Inadequate clinical and laboratory methods make it difficult to predict whether neurosyphilis will develop and what form it will take, although examination of the cerebrospinal fluid (CSF) can detect early asymptomatic neurosyphilis.

In recent years auditory tests have been used extensively to evaluate the function of the brain stem. Although pure-tone and speech audiometry are usually normal in patients with brain-stem lesions, refined audiological tests are often abnormal in such cases. Impedance audiometry and sound localisation tests have great potential for detecting brain-stem lesions, if the lesion affects the auditory pathways.[1] [2]

Brain-stem electrical response (BSER) audiometry (or ABR, auditory brain-stem response) is an even more sensitive test for brain-stem lesions. The aim of BSER audiometry is to record potentials that arise in the auditory pathways as a result of stimulation by sound. In a normal BSER five reproducible waves are distinguished (fig 1). Wave I is generated in the cochlear nerve, wave II in the cochlear nuclei in the brain stem, wave III in the superior olive in the pons, wave IV in the lateral lemniscus, and wave V in the inferior collicle in the mesencephalon.[3] BSER audiometry can detect different brain-stem lesions, such as intra-axial brain-stem tumours and brain-stem infarction,[4] [5] and multiple sclerosis.[6]
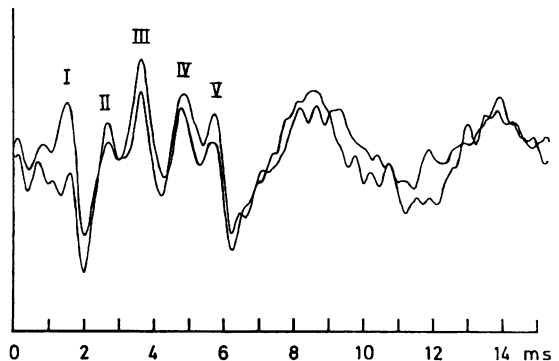
FIG 1 *BSER wave patterns from a patient with secondary syphilis. Unfiltered clicks with an intensity of 80 dB HL are used as stimuli. One stimulation round comprises 1024 stimuli. The repetition rate is 25 stimuli per second. Two identical stimulation rounds are superimposed on the graph. The responses from this patient have a normal appearance. Waves I-V are distinguished and marked on the graph. Each wave consists of a positive peak directed upwards followed by a negative peak directed downwards. The latencies and amplitudes of all waves are within normal limits.*

In the present study, auditory brain-stem responses were recorded in patients with secondary and latent syphilis with no clinical symptoms of neurosyphilis and in patients with general paralysis and congenital syphilis and in a normal control group matched for sex and age.

Patients

MEN
Seven men with secondary syphilis and four with latent syphilis were studied. Their mean age was 32

years (range 23-45 years). Secondary syphilis was diagnosed by clinical and laboratory findings. Latent disease was diagnosed by serological tests, which included the Wassermann reaction and the Kline, Venereal Disease Research Laboratory (VDRL), fluorescent treponemal antibody-absorption (FTA-ABS), and *Treponema pallidum* immobilisation (TPI) tests.

WOMEN

BSER audiometry was carried out on two women, one with congenital syphilis and one with general paralysis.

Case 1 was a 49-year-old woman whose mother was treated for syphilis when the patient was born. She developed epilepsy when aged 17; there were no syphilitic lesions of the skin, teeth, or eyes. In 1953, in connection with cholecystography, routine serological tests for syphilis showed positive results to the WR (1/60), the Kline test (+ + +), and the Meinicke test (+ + +). In 1962 she was treated with penicillin, after which the results of the WR and Kline test became negative, that of the Meinicke test +, and of the TPI test 100% immobilisation. At the present admission, the WR continued to give a negative result; the result of the VDRL test was ±, that of the IgG-FTA-ABS test positive (1/25), that of the IgM-FTA-ABS test negative, and that of the TPI test positive (100%). Analysis of the CSF showed that the routine test results, including electrophoresis, were within normal limits and those of the WR and TPI and FTA-ABS tests were negative.

Case 2 was a 71-year-old woman, who in 1931 had clinical signs of secondary syphilis and a positive Wassermann reaction; she was treated with bismuth and neosalvarsan. In 1941 test results for syphilis were positive in the CSF. Facial paresis and dysarthria appeared. Since 1942 the patient has been treated in a mental hospital for general paralysis with increasing dementia, hallucinations, and megalomania. In 1969 the patient showed stereotypy and became mutistic. Results of serological tests were then: WR and Kline and Meinicke tests negative, and TPI test positive (50-100%).

Methods

Routine pure-tone and speech audiometry was performed on all patients except case 2, who did not co-operate well enough for speech audiometry. Impedance audiometry was performed according to the principles described by Lidén *et al*.[7] Directional hearing was tested with phase audiometry[8] or with free-field directional audiometry.[9]

BSER AUDIOMETRY

Brain-stem electrical response (BSER) audiometry was performed on all the patients. In BSER audiometry a synchronised discharge in the auditory system is elicited by brief acoustic impulses. The discharge is picked up by two surface electrodes and amplified. A microcomputer calculates the averaged responses of 1000 or more single discharges. The method used in the present study is described elsewhere.[10]

From the averaged responses obtained at an intensity of 80 dB HL, the latencies and amplitudes of waves I, III, IV, and V were measured (fig 1). Each wave amplitude was measured in μV from a forehead-positive peak (P_n) to the following forehead-negative peak (N_n). Different ratios between the wave amplitudes were calculated. The following amplitude quotients were studied:

Wave IV-V (largest peak) divided by wave I $\dfrac{(P_{4 \cdot 5} N_5)}{P_1 N_1}$;

Wave IV-V (largest peak) divided by wave III $\dfrac{(P_{4 \cdot 5} N_5)}{P_3 N_3}$;

Wave V divided by the amplitude P_4 to N_5 $\dfrac{(P_5 N_5)}{P_4 N_5}$;

Wave V divided by wave IV $\dfrac{(P_5 N_5)}{P_4 N_4}$.

The latencies and the amplitude quotients from the 10 male patients with secondary or latent syphilis, all of whom had normal tympanic membranes, were compared with those of a control group of 23 healthy male volunteers. From each individual, only one ear, the one with the most distinct BSER patterns, was selected for the amplitude-ratio study. One ear was excluded to avoid problems with dependent observations. In six of the patients with syphilis the amplitudes of the right ear were measured and in four those of the left ear. In the controls the amplitudes of the right ear were measured in 14 and those of the left ear in nine.

STASTICAL ANALYSIS

Fisher's permutation test was used in the statistical analysis. A group subdivision was performed with respect to the number of measurements after which the comparisons were pooled over the groups.[11 12]

Results

SECONDARY AND LATENT SYPHILIS
Pure-tone and speech audiometry
The pure-tone thresholds were normal in 10 patients. In one patient the right ear had normal hearing up to 3000 Hz but a steep high-frequency loss reaching

80 dB at 6000 Hz. The hearing capacity of the other ear was normal. Speech perception was normal in all 11 patients.

Sound-localisation tests

Phase audiometry was performed in eight patients. The test was slightly abnormal in two patients, who were not, however, perfectly motivated for this rather difficult psycho-acoustic test. A free-field localisation test was performed on two further patients and was normal in both.

Impedance audiometry

The stapedius reflex thresholds were estimated in seven patients and all were within normal limits.

BSER audiometry

Latencies: the latencies for all five BSER waves were estimated for the intensity 80 dB HL as well as for lower levels in most cases. In seven of the patients the latencies of all waves were within normal limits. The latency of wave V at 80 dB HL for these patients varied between 5·4 ms and 5·7 ms (normal value: 5·51 ± 0·17 ms). The difference in time between wave I and wave V (I-V interval) varied between 4·0 ms and 4·3 ms (normal value: 4·03 ± 0·17 ms). In the other four patients the response from the inferior collicle (wave V) was bilaterally slightly delayed, with latencies varying between 5·9 ms and 6·2 ms (fig 2).

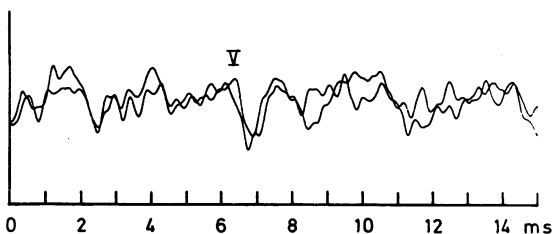The IV-V:I ratio varied from 0·63 to 2·03, and for five patients the quotient was lower than 1·0.

FIG 2 *BSER wave patterns (left ear) from a patient with latent syphilis. The latency of wave V is prolonged (6·2 ms at 80 dB HL. Normal value: 5·51 ± 0·17 ms).*

Amplitudes: the amplitude quotients from 10 of the patients with syphilis were compared with those of the control group (for one patient the amplitudes could not be estimated because of electroencephalographic and myogenic disturbances: the quotient $\frac{P_{4·5}\ N_5}{P_1\ N_1}$ was significantly lower in those with syphilis than in the normal group (0·05>P>0·01); the quotient $\frac{P_{4·5}\ N_5}{P_3\ N_3}$ showed no significant difference

between the two groups; the quotient $\frac{P_5\ N_5}{P_4\ N_5}$ was significantly lower in the patients with syphilis than in the normal group (0·05>P>0·01); and, finally, the quotient $\frac{P_5\ N_5}{P_4\ N_4}$ was significantly lower in those with syphilis than in the controls (0·01>P>0·001).

The analysis only applies to the two groups as groups and does not permit firm conclusions about the individuals within the group with syphilis. However, at least four of the patients with syphilis clearly had normal amplitude quotients (fig 1). The remaining six patients apparently had one or more abnormal quotients, although no normal figures can be presented. Some of these patients had remarkably small waves IV-V compared with wave I (fig 3 A and B).
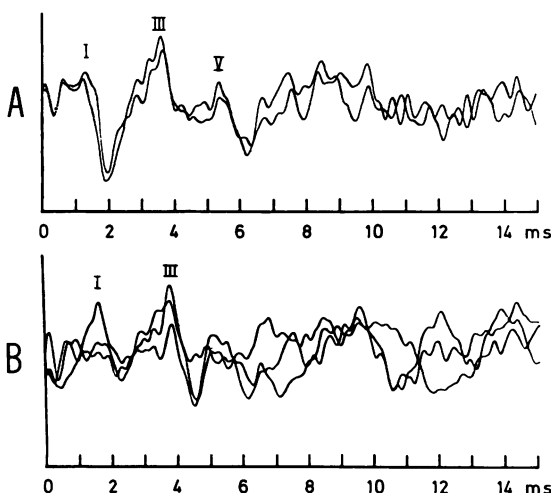
FIG 3 *(A) BSER wave patterns from a patient with secondary syphilis. The amplitude of wave V, normally the largest peak, appears diminutive compared with those of waves I and III. (B) BSER wave patterns from another patient with secondary syphilis. Waves I and III are clearly distinguished, but waves IV and V are small and poorly reproducible.*

The IV-V: I ratio varied from 0·63 to 2·03, and for five patients the quotient was lower than 1·0.

ADVANCED SYPHILIS

Case 1 (congenital syphilis)

This patient had a slight bilateral high-frequency loss and a dip of 35 dB at 2000 Hz for the right ear. Speech perception and directional hearing were normal.

The latency of wave V was bilaterally slightly prolonged (5·8 ms). The I-V interval was 4·3 ms for

the right ear and 4·4 ms for the left ear. When the left ear was stimulated, waves IV and V had significantly decreased amplitudes (fig 4A); the amplitudes of all BSER waves appeared normal when the right ear was stimulated (fig 4B). The findings indicated a discrete brain-stem lesion.

Case 2 (general paralysis)
This patient co-operated poorly on the psycho-acoustic tests. However, pure-tone audiometry indicated normal hearing, and no hearing loss exceeding 30 dB at any frequency was present.

The BSER was clearly pathological for both ears. Waves I and II were recognisable bilaterally, and their latencies were normal. Wave III had normal latency when the right ear was stimulated and a slightly prolonged latency when the left ear was stimulated. In the left ear, wave V was clearly distinguished in all averaged responses, and the latency of this wave was significantly prolonged, reaching 6·1 ms (fig 5). The I-V interval was also significantly prolonged (4·7 ms). When the right ear was stimulated no consistent reproducible waves IV and V were found. These BSER findings indicated a brain-stem lesion.
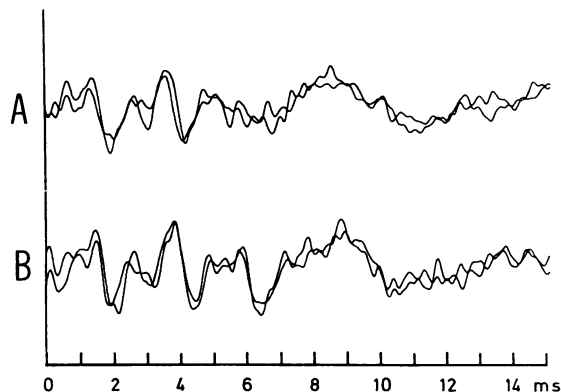

FIG 4   *BSER wave patterns from a patient with congenital syphilis (case 1): those from the left ear (A) show that wave V has a very small amplitude compared with the other waves; in those from the right ear (B) all waves appear normal.*

Discussion

In the present study the two patients with advanced syphilis showed clear BSER abnormalities indicative of a brain-stem lesion. In the patient with general paralysis, prolongation of BSER-wave latencies and
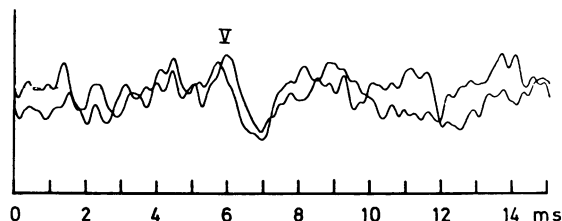

FIG 5   *BSER wave patterns (left ear) from a patient with general paralysis (case 2); wave V has a prolonged latency.*

absence of the colliculus-inferior response from one ear indicated a lesion in the brain stem. The patient with congenital syphilis had very discrete signs of brain-stem involvement.

All 11 patients with secondary or latent syphilis had preserved BSER waves with normal or slightly prolonged latencies. The amplitude quotients were calculated for 10 of these patients and they were slightly abnormal in many cases, indicating a subclinical brain-stem lesion caused by the disease.

The IV-V: I ratio was conspicuously small in many of the patients with syphilis. Starr and Achor[4] estimated the relative amplitudes of some BSER waves in the same averaged response. They found that a IV-V: I ratio less than 0·5 was abnormal, and a ratio between 0·5 and 1·0 was suggestive of central auditory pathway dysfunction. In this study half the patients with secondary or latent syphilis had a ratio between 0·5 and 1·0. Moreover, Rosenhamer *et al*[13] found a mean V: I ratio of 1·55 at 80 dB SL for a group of normal individuals. The variation was considerable, but wave V was significantly the largest peak in their study. Even if it is not possible to compare directly results from different BSER audiometry laboratories, these studies support the present observation that patients with syphilis often have abnormally small IV-V waves.

Abnormalities within the IV-V complex have not generally been studied. Rosenhall *et al*[14] have found that wave V might be very small compared with wave IV, or that N_4 might be very deep, reaching the same value as N_5, in patients with known brain-stem lesions. In the present study, these two abnormal patterns were often seen in the patients with syphilis. Thus, the quotients $\frac{P_5 N_5}{P_4 N_5}$ and $\frac{P_5 N_5}{P_4 N_4}$ were significantly lower in those with syphilis than in the controls, and this discrepancy was especially pronounced for the latter quotient. These findings, together with the findings of prolonged wave V latencies in some patients, support the concept that discrete brain-stem dysfunction is present in patients with syphilis.

Involvement of the central nervous system early in the course of a syphilitic infection may sometimes give neurological symptoms. Only about 15% of the patients in the secondary stage show abnormalities in the CSF.[15] The manifestations of early neurosyphilis are varied and appropriate laboratory tests are essential to confirm or disprove clinical suspicion of its presence. Determination of auditory brain-stem responses is an easy and painless method of showing alterations in the brain stem due to syphilis.

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